

REMARKS

Applicant respectfully requests entry of amendments to claims 7, 16, 17, 20, 21, 23, and 25. Support for the amendments can be found throughout the specification, including Tables I and II, page 11, line 1, sequence identifiers (SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, and the sequence listing), and the originally filed claims, and, therefore, do not add new matter.

Applicant submits that pending claims 7 and 16-28 are in condition for allowance, or are in better condition for presentation on appeal.

Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 7 and 16-28 stand rejected under 35 U.S.C. §112, second paragraph as allegedly being indefinite.

Applicant traverses the rejection, including as it might apply to amended claims 7, 16, 17, 20, 21, 23, 25, and claims dependent therefrom, for the reasons given below.

Claim 7 no longer recites "TNFSF polypeptide," so the rejection is rendered moot. Applicant has amended the claim to recite "TNFSF ligand." The term "TNFSF ligand" is a term of art and would be known to one of skill in the art generally as a protein having an intracellular N-terminal domain, a short transmembrane segment, an extracellular stalk, and a globular TNF-like extracellular domain, which ligands bind to their cognate receptors.¹ Further, one of skill in the art would know of soluble forms of the ligand, which do not comprise the short transmembrane domain. Moreover, one of skill in the art would know that such ligands generally form homo- or hetero-trimeric complexes. These properties are recited on page 3 of the instant application, as well as throughout the specification. As such, one of skill in the art would understand the metes and bounds of the term.

¹ See, e.g., < <http://www.ncbi.nlm.nih.gov/Structure/cdd/cddsrv.cgi?uid=cd00184>>, last visited, December 15, 2005.

Regarding claims 16 and 17, while Applicant does not acquiesce to the reasoning offered in the Office Action, and to expedite prosecution toward allowance, claims 16 and 17 have been amended to no longer recite the disputed term.

Regarding claims 17, 21, and 23, while Applicant does not acquiesce to the reasoning offered in the Office Action, and to expedite prosecution toward allowance, claims 17, 21, and 23 have been amended to recite the full meanings of the acronyms as identified in the Action.

For these reasons, Applicant respectfully requests that the rejection be withdrawn.

Rejections Under 35 U.S.C. §112, First Paragraph

Claims 7, 16, and 17 stand rejected under 35 U.S.C. §112, first paragraph as allegedly lacking written description support.

Applicant traverses the rejection, including as it might apply to amended claims 7, 16, 17, 20, 21, 23, 25, and claims dependent therefrom, for the reasons given below.

The Office Action alleges, in pertinent part, that as the specification does not disclose polypeptide sequences of other TNFSF proteins, nor does the specification describe various trimer units that will be linked to the TNFSF, the written description is not commensurate in scope with the recitation of the claims, *per se*. Further, the Action alleges that with the exception of CD40L, T147N modification of CD40L, and RANKL/TRANCE (this statement ignores the disclosure at page 32, where SPD-CD27L/CD70 polypeptides were prepared), the skilled artisan cannot envision all the detailed chemical structure of the claimed polypeptide, intimating that only “[t]he polypeptide itself” can meet the standard for adequate written description. Applicant respectfully submits that such allegations are incorrect.

Notwithstanding the amendments to the claims, to suggest that the specification neither describes various trimer units that will be linked to the TNFSF nor discloses other TNFSF proteins is to ignore Tables I and II, and to disregard the meaning of the art recognized term “collectins.” Collectins are proteins which possess C-type lectin (CTL) domains, where these latter domains function as carbohydrate binding modules known as carbohydrate recognition domains (CRDs). It is also art recognized that such collectins associate with each other through

several surfaces to form dimers, trimers, and tetramers. Since the specification as filed 1) recites the collectins of Table II, whose structure/function properties were well known,² and 2) provides GenBank accession numbers for the various TNFSF ligands in Table I, it is not clear as to how the Action has come to this position.

Nevertheless, the position taken in the Office Action in view of the cited case law is inapposite in that none of the cases recited in the Action support a written description standard which requires a re-description of what was already known. For example, in Fiers v. Revel, 25 U.S.P.Q.2d 1601, 1604, 984 F.2d 1164, at 1171 (Fed. Cir. 1993), much of the DNA sought to be claimed was *of unknown structure*, whereby the court viewed the breadth of the claims as embracing a “wish” or a research plan. In Amgen Inc. v. Chugai Pharmaceutical Co., Ltd., 18 U.S.P.Q.2d 1016, 1021, 927 F.2d 1200, at 1206 (Fed. Cir. 1991), the court explained that *a novel gene* was not adequately characterized by its biological function alone because such a description would represent a mere “wish to know the identity” of the novel material. In Fiddes v. Baird, 30 U.S.P.Q.2d 1481, at 1483 (Bd. Pat. App. & Int. 1993), the court explained that the state of the art at the time the invention was filed, where the inventor only disclosed an amino acid sequence and *a theoretical DNA sequence*, there was inadequate knowledge concerning the relationship between gene structure and proteins for the theoretical sequence to be used to establish possession. For the instant invention there are no theoretical sequences, and the sequences disclosed in the instant specification are already known, including recognized structure/function relationships between recited genes and their corresponding encoded proteins/domains. Thus, the present facts are distinguishable.

On the other hand, in Capon v. Eshhar, 76 U.S.P.Q.2d 1078, 1085, 418 F.3d 1349, at 1357 (Fed. Cir. 2005), the court stated that requiring sequences for chimeric genes to be fully presented, although the sequences of the component genes are known, is an inappropriate generalization. The court reasoned that when the prior art includes sequence information, there is no *per se* rule that the information must be determined afresh. Id. As in Capon, the present invention is not in the discovering of which segments of some unknown or “wished for”

² See, e.g., < <http://www.ncbi.nlm.nih.gov/Structure/cdd/cddsrv.cgi?uid=cd00037>>, last visited December 15, 2005.
GT\6470823.3
328342-179

sequence might be related to a specific function, but in the novel combination of the segments of known genes to achieve a novel result (Id., at 1357); a result that the Action itself admits is novel (i.e., “[n]o claims are allowable but they are apparently free of the prior art,” at page 7, Item 10 of the Action). Thus, in concurrence with the Court of Appeals for the Federal Circuit in Capon, Applicant submits that the requirement that chimeric polypeptides prepared from known sequences of known function must be analyzed and reported in the specification is not the standard for written description. Id.

Accordingly, the claims as presently recited describe 1) the orientation of the sequences making up the polypeptides, 2) the order of the requisite domains in the polypeptide, and 3) the minimal and maximal lengths of the included domains for the polypeptide (i.e., the collectin polypeptide minus the CRD or the TNFSF polypeptide minus the intracellular and transmembrane domains), where the structure/function of the domains and polypeptides disclosed in the invention are *defined and well known in the art*. As such, one of skill in the art could envision the chemical details of the polypeptide of the claimed invention, and would appreciate that the inventors were in possession of the genus as claimed at the time the invention was filed.

For these reasons, Applicant respectfully requests that the rejection be withdrawn.

Claims 7, 16, and 17 stand rejected under 35 U.S.C. §112, first paragraph as allegedly lacking enablement.

Applicant traverses the rejection, including as it might apply to amended claims 7, 16, 17, 20, 21, 23, 25, and claims dependent therefrom, for the reasons given below.

The Office Action alleges, in pertinent part, that while the specification is enabling for CD40L-SPD, T146N-CD40L-SPD, and RANKL/TRANCE-SPD, the specification is not enabling for other fusion polypeptides consisting of TNFSF functional equivalents, and modifications thereof (this statement also ignores the disclosure at page 32, where SPD-CD27L/CD70 polypeptides were prepared).

As the amended claims no longer recite “functional equivalents,” this aspect of the rejection is rendered moot. However, the Action goes on to allege that the specification as filed

1) fails to disclose any other fusion polypeptide, 2) fails to provide any guidance regarding the generation of fusion polypeptides which retain function, and 3) fails to provide detailed information regarding the structural and functional properties from the sequence data presented. The Action further intimates that due to the unpredictability of protein structure and function, undue experimentation would be required for the skilled artisan to practice the full scope of the invention. Applicant respectfully submits that such allegations are incorrect.

While it is appropriate to recognize variability in determining the scope of invention, determination of what is needed to support generic claims to biological subject matter depends on a variety of factors including 1) knowledge in the particular field, 2) the extent and content of the prior art, 3) the maturity of the science or technology, and 4) the predictability of the aspect at issue. Capon v. Eshhar, 76 U.S.P.Q.2d 1078, 1084, 418 F.3d 1349, at 1356 (Fed. Cir. 2005).

The present invention represents more than “a mere germ of an idea,” the specification supplies the novel aspects of the invention, and construction of multimeric immunologic chimeric polypeptides is certainly not in the early stages of development (e.g., page 2, line 10 to page 7 line 1). (See, also, Genentech, Inc. v. Novo Nordisk, 42 U.S.P.Q.2d 101, 108 F.3d 1361 (Fed. Cir. 1997)). Further, in the present specification, not only are the general teachings of how to select and recombine the requisite domains disclosed (e.g., page 19, line 19 to page 20, line 11), but also specific examples are provided for the production of specified chimeric genes (e.g., Example 1, at page 28 and page 32, lines 4-6). Moreover, standardized description and identification, including known procedures for selecting, isolating, and linking known DNA segments containing well recognized domains, whose structure/function relationships are known, are disclosed (e.g., page 20, line 13 to page 24, line 2; and page 28, line 4 to page 29, line 2). And while such procedures involve some level of technical manipulation, because such methods and steps are routinely used in the art, such procedures do not rise to the level of undue experimentation. (See, e.g., Johns Hopkins University v. Cellpro, Inc., 47 U.S.P.Q.2d 1705, 152 F.3d 1342 (Fed. Cir. 1998), where the court stated that “experimentation does not constitute undue experimentation” where “it is merely routine.”).

Regarding unpredictability, it is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that

the effect is sufficiently demonstrated to characterize the generic invention. See, e.g., In re Angstadt, 537 F.2d 498, 504 (CCPA 1976). Accordingly, generic inventions are not *per se* invalid because success for each possible iteration is not assured. Capon, at 1357.

Regarding the Wands factors, 1) sequence information for each component of the chimeric polypeptide was provided by the prior art, including structure and function data for the recited domains, and the specification clearly describes the collectins by art recognized identifiers (Table II), as well as TNFSF sequences by GenBank accession number (Table I); 2) the domains comprising the chimeric polypeptide were provided by the prior art, including structure/function relationships and domain boundaries, and the specification discloses the orientation and requisite order of the domains comprising the chimeric polypeptide (e.g., page 28, lines 4 to page 29, line 2, and Figure 1); 3) as stated above, construction of multimeric immunologic chimeric polypeptides is not in the early stages of development (e.g., page 2, line 7 to page 7, line 1); 4) the level of skill in the art is high, and such a skilled artisan would have the knowledge and capabilities of using the information provided in the specification to make and use the invention commensurate in scope with the amended claims (e.g., search sequence databases, use standard cloning techniques to conjoin DNA sequences, produce recombinant proteins from eukaryotic hosts comprising expression vectors, etc.); 5) the specification provides examples of polypeptides with predicted function, including the generation of a control chimeric polypeptide that maintained the functionality of the parent TNFSF (i.e., remained inactive due to a point mutation even after the TNFSF domain was incorporated into a chimeric polypeptide as predicted: see Example 2, at page 29, Example 6, at page 31, and Figure 6); 6) as stated above, standardized description and identification, including known procedures for selecting, isolating, and linking known DNA segments containing well recognized domains, whose structure/function relationships were known, are disclosed to provide direction to the skilled artisan (e.g., page 20, line 13 to page 24, line 2; and page 28, line 4 to page 29, line 2); 7) at least 3 working examples of functional chimeric polypeptides (e.g., SPD-CD40L, SPD-CD27L/CD70, and SPD-RANKL/TRANCE) are disclosed; and 8) as stated above, the procedures used to practice the invention are merely routine (e.g., see Example 1, at page 28), and such procedures do not rise to the level of undue experimentation.

In re Application of:
Kornbluth
Application No.: 09/454,223
Filing Date: December 09, 1999
Page 14

PATENT
Attorney Docket No. UCSD1590

Therefore, the claims are enabled because the specification provides appropriate guidance, working examples, and prediction of function based on observed properties of the claimed polypeptide such that one of skill in the art could practice the invention as claimed, in the absence of undue experimentation.

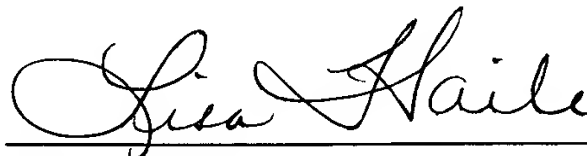
For these reasons, Applicant respectfully requests that the rejection, including as it may be applied to the amended claims, be withdrawn.

Conclusion

In view of the above amendments and remarks, Applicant submits that pending claims 7 and 16-28 are in condition for allowance, or are in better condition for appeal. The Examiner is invited to contact Applicant's undersigned representative if there are any questions relating to this submission. The Commissioner is hereby authorized to charge any fees that may be associated with this communication, or credit any overpayment to Deposit Account No. 07-1896.

Respectfully submitted,

Date: December 20, 2005



Lisa A. Haile, J.D., Ph.D.
Registration No. 38,347
Telephone: (858) 677-1456
Facsimile: (858) 677-1465

DLA Piper Rudnick Gray Cary US LLP
4365 Executive Drive, Suite 1100
San Diego, California 92121-2133
USPTO Customer Number 28213